

b) determining if said patient is predisposed to develop severe disease based on said information and the presence or absence of a polymorphism in an HLA-DRB1 allele in said patient.

49. The method of claim 48, wherein said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells comprises the percent of CD4<sup>+</sup> cells that are CD28 negative.
50. The method of claim 48, wherein said reference frequency is derived from the CD4<sup>+</sup>/CD28<sup>null</sup> cell frequency from a population.
51. The method of claim 50, wherein said population comprises a population of patients having a diffuse rheumatoid arthritis condition.
52. The method of claim 50, wherein said population comprises a population of patients having a follicular rheumatoid arthritis condition.
53. The method of claim 50, wherein said population comprises a population of patients having a granulomatous rheumatoid arthritis condition.
54. The method of claim 50, wherein said population comprises a population of healthy individuals.
55. The method of claim 50, wherein said population comprises a population of patients having subcutaneous nodules.
56. The method of claim 50, wherein said population comprises a population of patients having extra-articular involvement.
57. The method of claim 50, wherein said population comprises a population of patients having major joint destruction.

58. The method of claim 48, wherein said polymorphism comprises an HLA-DRB1 allele that encodes a polypeptide having an uncharged amino acid at position 74.

59. The method of claim 48, wherein said polymorphism comprises an HLA-DRB1 allele that encodes a polypeptide free from negatively charged amino acids at positions 70 and 71.

60. A method for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said method comprising:

- a) determining the frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient,
- b) determining the presence or absence of a polymorphism in an HLA-DRB1 allele in said patient,
- c) comparing said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells to a reference frequency to obtain information about said rheumatoid arthritis condition, and
- d) determining if said patient is predisposed to develop severe disease based on said information and said presence or absence of said polymorphism.

61. A kit for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said kit comprising:

- a) a first binding pair member, wherein said first binding pair member has specific binding affinity for a CD4<sup>+</sup>/CD28<sup>null</sup> cell marker such that the frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient is determinable, and
- b) an oligonucleotide primer, wherein said oligonucleotide primer has specific binding affinity for at least a portion of the locus containing an HLA-DRB1 allele such that the a polymorphism of said HLA-DRB1 allele in said patient is determinable.

62. The kit of claim 61, wherein said kit comprises a reference chart, wherein said reference chart contains information about CD4<sup>+</sup>/CD28<sup>null</sup> cell frequencies such that said predisposition is determinable based on said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient and said polymorphism of said HLA-DRB1 allele.--

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